

Effect of a Probiotic Strain on Gut Microbiota and Cytokines in Inflammatory Bowel Disease: A Double Blind Randomized Placebo Controlled Study

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Introduction

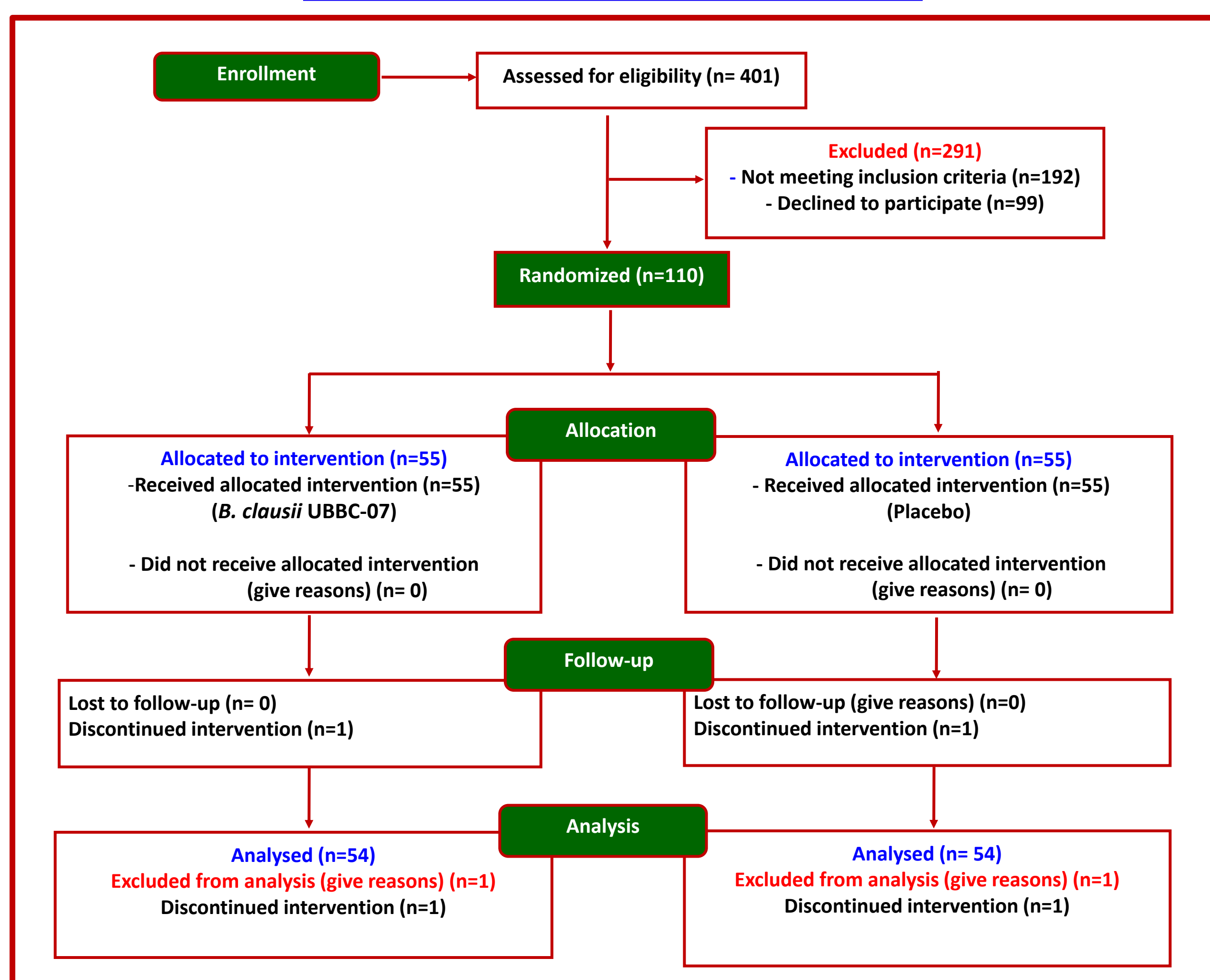
Gut maintains homeostasis but in inflammatory bowel disease (IBD) this homeostasis gets disturbed and leads to intestinal inflammation. IBD is a multi-factorial disease which involves individual's genetics, lifestyle, immunity and gut microbiota. Microbial interventions using probiotics to maintain the microbial homeostasis is an important preventive and therapeutic approach for different diseases including IBD. Therefore, a double blind, randomized placebo controlled study was conducted to assess the effect of a probiotic *Bacillus clausii* UBBC-07 along with standard medical treatment (SMT in the IBD patients (CTRI registration- Ref-CTRI/2019/11/022087).

Material & Method

- A double blind, randomized placebo controlled study was conducted at All India Institute of Medical Sciences, New Delhi to assess the effect of *Bacillus clausii* UBBC-07 in Indian IBD patients (18–60 years) under standard Medical treatment (SMT) with ethical approval (AIIMS-IEC-Ref – IEC.478/07.10.2016.OP-7).
- After required screening (as per inclusion / exclusion criteria) of the clinically confirmed patients of IBD, a probiotic capsule (CFU-2X10⁹ per capsule) / placebo twice in day for the duration of 4 weeks were given to the each enrolled patient.
- Patients were assessed before and after intervention for clinical features, physical symptoms, gut microbiota, cytokines and other biochemical parameters.

Results & Discussion

'CONSORT' Flow Diagram

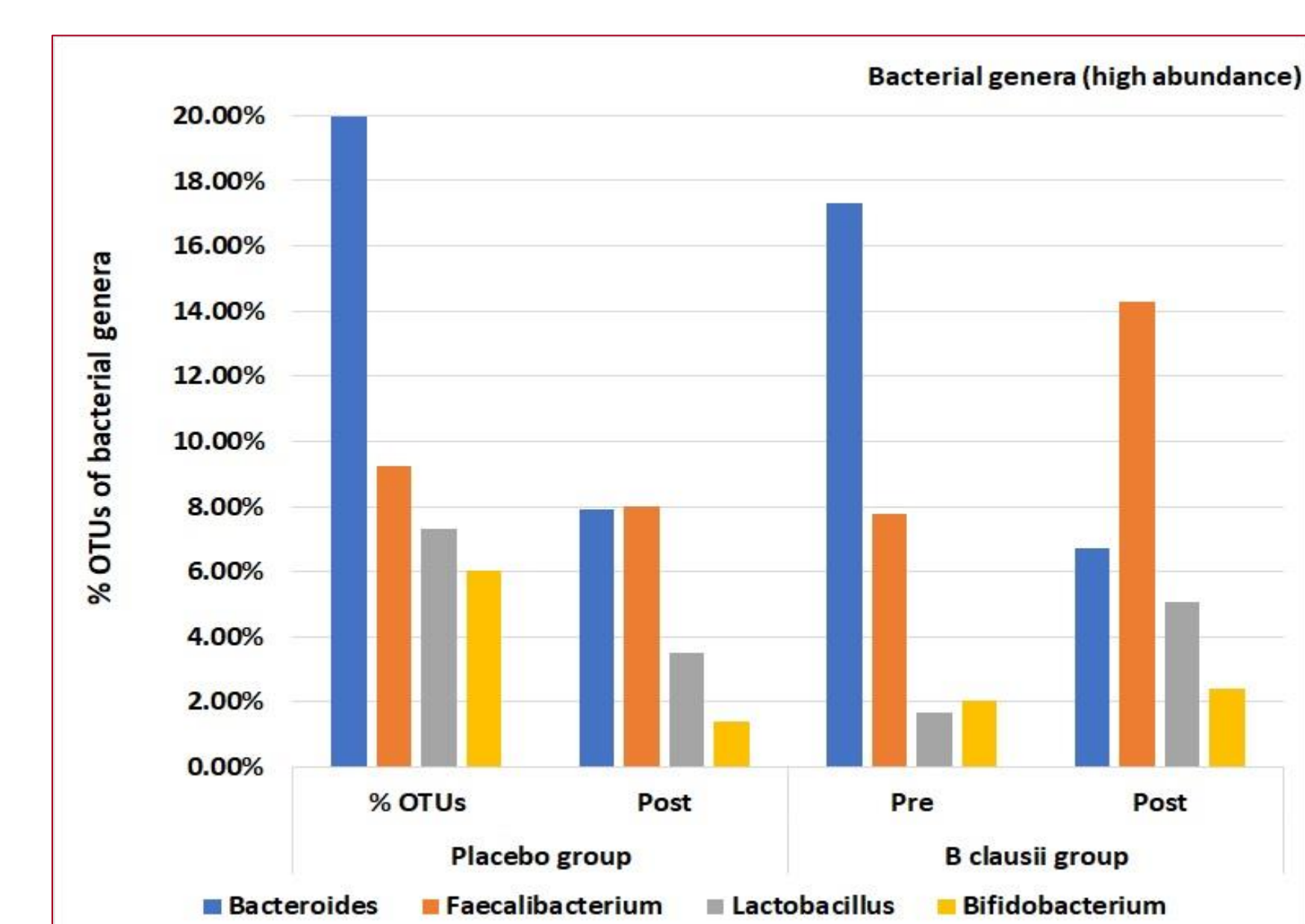
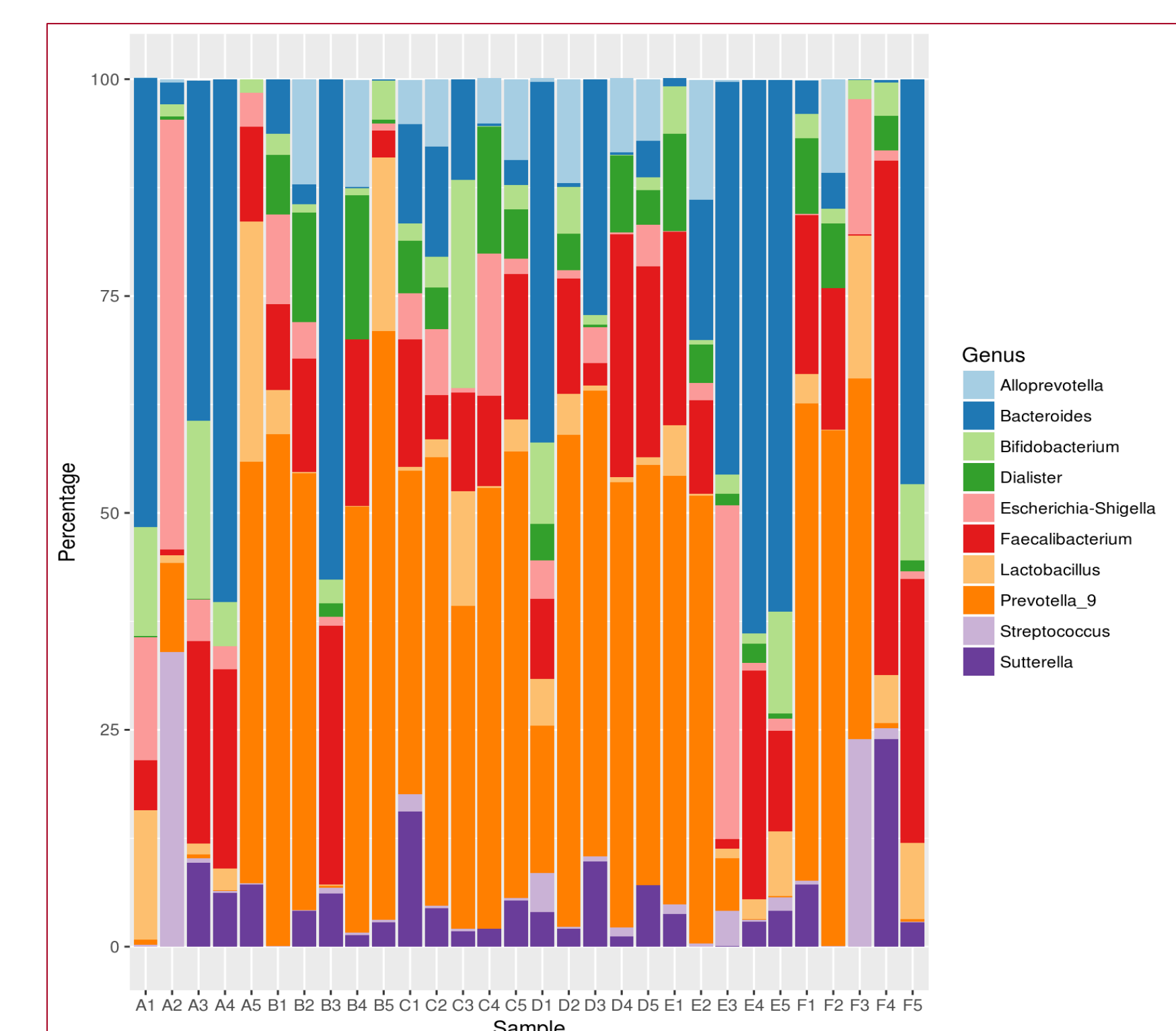
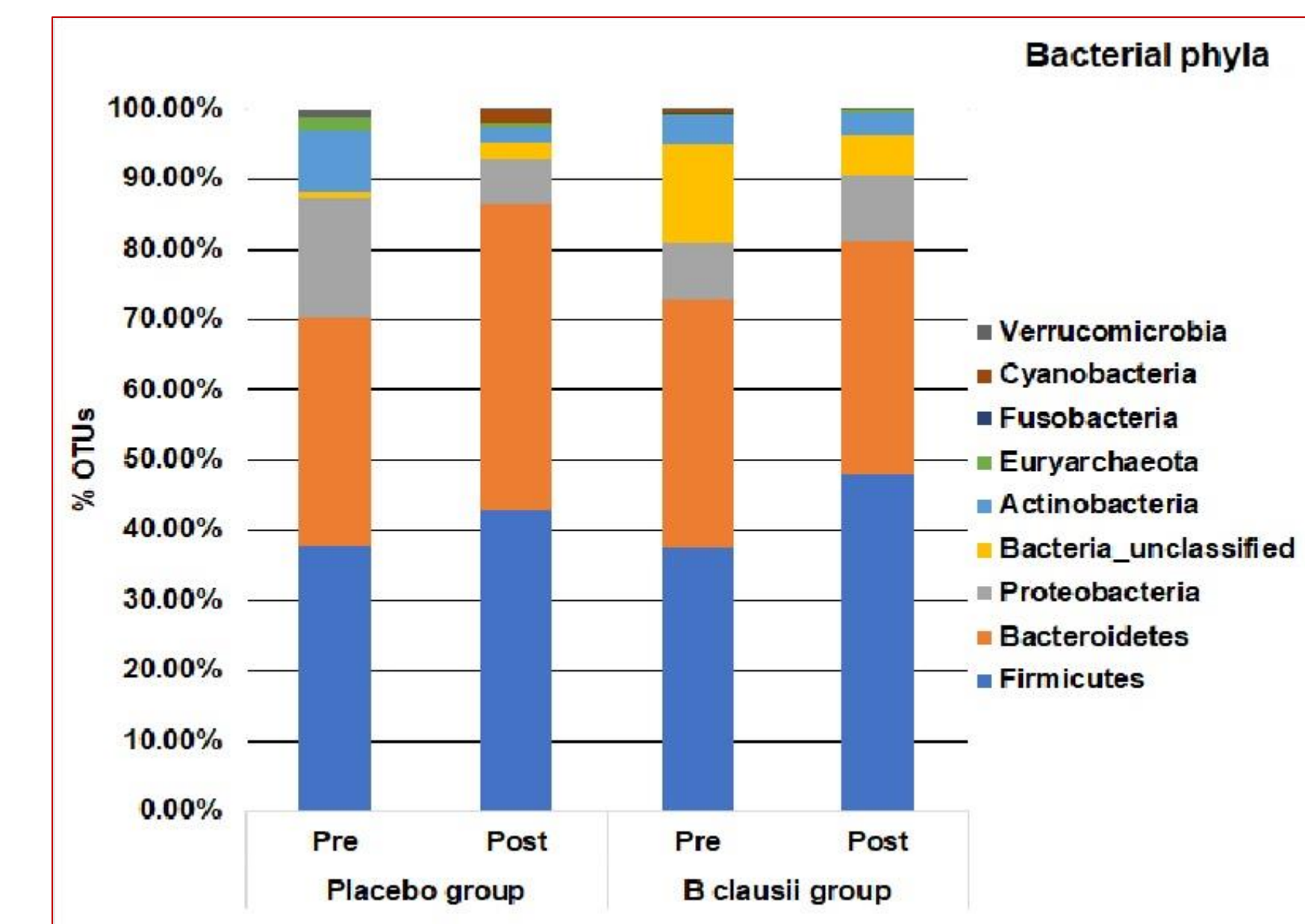


Serum Cytokines, serotonin and dopamine levels in pre and post intervention samples in treatment and placebo group

Cytokine (pg/ml)	<i>Bacillus clausii</i> UBBC-07 group			Placebo group		
	Pre	Post	P value	Pre	Post	P value
UC patients						
IL-10	21.6±4.8	31.5±5.2	<0.05	23.5 ± 3.9	22.6 ± 7.5	NS
IL-6	44.5 ± 5.6	31.5 ± 4.4	<0.05	45.4 ± 6.2	40.6 ± 4.2	NS
IL-17	39±6.3	24.5±4.5	<0.05	38.8± 6.2	41.9 ± 4.6	NS
IL-23	898.5 ± 54.6	805.6 ± 46.7	NS	906.8 ± 68.3	897.02 ± 73.5	NS
IL-1β	384±45.5	246±38.4	<0.05	352.5 ± 67.6	386.7 ± 56.2	NS
TNF- α	65.6 ± 6.2	58.3 ± 5.6	NS	75 ± 5.2	68.5 ± 9.5	NS
CD patients						
IL-10	18.4 ± 4.86	28.4 ± 4.9	<0.05	22.2 ± 4.1	25.6 ± 6.6	NS
IL-6	44.4 ± 4.8	38.4 ± 7.2	NS	43.5 ± 5.6	46.7 ± 4.8	NS
IL-17	45.4±4.8	28.6±7.4	<0.05	41.4 ± 12.4	43.6 ± 6.8	NS
IL-23	902.6±48.5	834.6±40.8	NS	911.5 ± 66.4	875.6 ± 56.5	NS
IL-1β	375.2±36.4	268±32.2	<0.05	445 ± 58.2	284.5± 48.5	<0.05
TNF- α	78.4 ± 6.2	65.3 ± 8.2	NS	66.2 ± 12.6	75.5 ± 10.8	NS
Serum serotonin and dopamine in both UC and CD patients						
Serotonin (ng/ml)	125.8±17.6	110.30±12.4	NS	121.5±16.50	106.8 14.65	NS
Dopamine (pg/ml)	9.25±3.22	10.45±3.5	NS	10.50±2.6	11.4±3.6	NS

- In the probiotic treated group, *Bacillus clausii* UBBC-07 was detected in 74.5 % and 79.6 % in the UC and CD patients respectively and the detection was significant (p <0.001) as compared to placebo group.
- In the treatment group, the average % OTUs of the phylum Firmicutes were 37.58 % and 48.0 % in the before and after intervention samples, respectively and in the treatment group's post-intervention sample, the abundance of the phylum Firmicutes increased significantly.
- In the treatment group, the average % OTUs of the phylum Bacteroidetes were 35.13 % and 33.14 % in before and after intervention samples, respectively. In post-intervention samples, the treatment group showed a drop in OTUs of the phylum Bacteroidetes.
- Among bacterial genera, the abundance of *Lactobacillus*, *Bifidobacterium*, *Faecalibacterium*, and *Alistipes* were increased and abundance of bacterial genera *Bacteroides*, *Dialister*, *Roseburia* and *Olsenella* were decrease in the post intervention samples in the treatment group.
- Significant increase was observed in IL-10 (p <0.05) and variable decrease in the secretion of IL-1β, IL-6, IL -17 and IL -23 in probiotic group.
- The SCCAI score was decreased in 42.52 % and 31.58 % of the UC patients post intervention in treatment and placebo group respectively and the difference was significant (p <0.05). There was no significant difference in CDAI score between treatment and placebo groups.
- In the probiotic group a significant decrease in the symptoms of IBD and improvement in the psychological parameter to various degrees was noted. Partial results of the study are published.

Bacterial abundance in study groups



Key Highlights

- (i) Firmicutes was increased and Bacteroidetes was decreased in probiotic group,
- (ii) *Lactobacillus*, *Bifidobacterium* and *Faecalibacterium* were increased
- (iii) Significant increase was observed in IL-10 in the probiotic treated group,
- (iv) In probiotic group decrease in the severity of symptoms of IBD was noted
- (v) Improvement in the psychological parameters was noted in probiotic group
- (vii) *Bacillus clausii* UBBC-07 along with SMT shown efficacy in IBD patients

Conclusion

Probiotic *Bacillus clausii* UBBC-07 showed good survival in IBD patients without any reported adverse event. An increase in the abundance of phylum Firmicutes and decrease in the Bacteroidetes was observed after intervention in the probiotic treated group. Significant increase was observed in the commensal anaerobic bacterial genera *Lactobacillus*, *Bifidobacterium* and *Faecalibacterium* in post intervention sample in the probiotic treated group. A significant increase in the IL-10 and variable decreased in the secretion of IL-6, IL-1β, TNF- α, IL -17 and IL -23 was observed in probiotic treated group. Probiotic strain *B clausii* UBBC-07 have shown efficacy in IBD patients by modulating gut microbiota, cytokines, decreased in the symptoms of IBD and improvement in the psychological parameter to various degrees.

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